IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF SOUTH CAROLINA
CHARLESTON DIVISION

IN RE: LIPITOR (ATORVASTATIN CALCIUM) MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION	MDL No. 2:14-mn-2502-RMG
This document relates to: All Cases	

PLAINTIFF'S REPLY SUPPLEMENTAL MEMORANDUM IN FURTHER OPPOSITION TO PFIZER'S MOTION TO EXCLUDE PLAINTIFFS' EXPERT TESTIMONY ON THE ISSUE OF GENERAL CAUSATION

H. Blair Hahn (Fed. I.D. # 5717)
RICHARDSON PATRICK WESTBROOK & BRICKMAN, LLC
1037 Chuck Dawley Blvd., Bldg. A
Mount Pleasant, SC 29464
Telephone: (843) 727-6500
Facsimile: (843) 727-6642
bhahn@rpwb.com

Plaintiffs' Lead Counsel

Ramon Rossi Lopez (CA 86361)
LOPEZ MCHUGH, LLP
100 Bayview Circle, Suite 5600
Newport Beach, CA 92660
Telephone: (949) 737-1501
Facsimile: (949) 737-1504
rlopez@lopezmchugh.com

Jayne Conroy (NY 8611)
SIMMONS HANLY CONROY LLC
One Court St.
Alton, IL 62002
Telephone: (618) 259-2222
Facsimile: (843) 7276642
jconroy@simmonsfirm.com

Plaintiffs' Executive Committee on behalf of the Plaintiffs' Steering Committee

February 19, 2016

TABLE OF CONTENTS

Page

INTRODUCTION

In its Supplemental Dose Brief in Further Support of Its Motion to Exclude Plaintiffs' Expert Testimony on General Causation ("Supp. Dose Br."), Pfizer takes issue individually with each and every scientific study showing that Lipitor causes diabetes, whether at 80 mg or at the lower therapeutic doses, 40 mg, 20 mg and 10 mg. Finding each study insufficient, on its own, to establish causation, Pfizer asks this Court to disregard the cumulative effect of *all* of the evidence. It also, once again, asks this Court to act as a fact-finder, weighing the evidence and reaching its own conclusion as to which of the eminent scientists who have been offered as experts to believe. Neither is appropriate on this *Daubert* motion.

First, Pfizer asks this Court to consider each relevant scientific study, and each type of study, in a vacuum, divorced from all the others. By Pfizer's reasoning, a pound of feathers can be treated as weighing nothing at all, because each individual feather is too light to take account of. By Pfizer's reasoning, each separate piece of a jigsaw puzzle would be discarded one by one as insufficient to create a picture on its own, and the picture that can emerge only from assembling the pieces together would forever remain hidden. What Pfizer cannot explain, however, is why there are *so many* consistent pieces, and so many types of pieces, that need to be explained away: Pfizer's original clinical trials, showing elevated glucose in subjects taking Lipitor; Pfizer's updated clinical trials, also showing elevated glucose in subjects taking Lipitor; Dr. Quon's mechanistic studies, also showing glucose metabolism changes in subjects taking Lipitor; the SPARCL study showing an increased risk of diabetes in subjects taking 80 mg of Lipitor; numerous clinical trials involving other statins showing increased risk of diabetes as a class effect of statins, so much so that, as reflected in peer-reviewed, published literature, there is a scientific consensus that statins can cause diabetes at some therapeutic doses; Pfizer's other studies, including TNT and IDEAL, also supporting a causal connection between

Lipitor and diabetes; Pfizer's ASCOT study, the meaning of which is the subject of expert disagreement, but which unquestionably showed an increased risk of diabetes at 10 mg doses of Lipitor, whether or not that increase was deemed statistically significant; meta-analyses of clinical trials, also finding a connection between Lipitor and other statins, on the one hand, and diabetes on the other; and, finally, multiple observational studies showing, in large populations, increased risk of diabetes in subjects taking Lipitor and other statins, even when controlling for possible confounding factors. Pfizer keeps throwing water on the smoke each time it rises, offering one explanation, then another, but the smoke keeps coming back: as Plaintiffs' experts explain, behind it all, there is, after all, a fire.

Second, the disagreement between the parties' experts cannot and ought not be resolved by the Court. Each of Plaintiffs' experts is a qualified and credentialed scientist; each has employed a valid and reliable scientific methodology, relying on published peer-reviewed literature, on clinical trials carried out by Pfizer, and on well-accepted, reliable methods for evaluating the underlying scientific evidence. Scientists disagree about the meaning of scientific studies, but when the parties' experts are using the same methodology and reaching different conclusions, the Federal Rules of Evidence provide no basis to exclude the opinions of either side. That the Court, *if it were the factfinder*, would believe one expert over another is beside the point: the Federal Rules ask the Court to set aside its own views as factfinder and act instead as gatekeeper, excluding only unreliable, unscientific opinions, rather than any opinion it finds unpersuasive.

As discussed below, and as previously set forth in Plaintiffs' Steering Committee Memorandum of Law in Opposition to Pfizer's Motion to Exclude Plaintiffs' Expert Testimony on The Issue of General Causation (as corrected, Doc. #1053), Plaintiffs' Steering Committee's Supplemental Memorandum of Law Concerning Expert Testimony (Doc. #1159), Plaintiffs' Steering Committee's Reply Memorandum of Law in Response to Pfizer's Post-Hearing Brief (Doc. #1166), and Plaintiff's Supplemental Memorandum

in Further Opposition to Pfizer's Motion to Exclude Plaintiffs' Expert Testimony on the Issue of General Causation (Doc. #1384), Pfizer's motion to exclude evidence of general causation should be denied in its entirety, and this battle of the experts should be resolved by a jury, as required under the Federal Rules of Evidence.

ARGUMENT

I. PLAINTIFFS' EXPERTS PROPERLY RELY ON THE TOTALITY OF CLINICAL TRIALS, META-ANALYSES, AND OBSERVATIONAL STUDIES SHOWING THAT LIPITOR CAN CAUSE DIABETES

Pfizer once again contends that no evidence exists that demonstrates Lipitor can cause diabetes at any dosage level. Thus, Pfizer continues to insist that, even with respect to the 80 mg dose, Plaintiffs' experts cannot tell the jury what numerous scientists have concluded based on epidemiological studies reported in peer-reviewed published articles: that statins elevate blood glucose levels, increase the risk of new onset diabetes, and can cause diabetes. Thus, as reported in the *Journal of General Internal Medicine* in 2015, "[t]he increased risk of new-onset type 2 diabetes in patients treated with statins has been *well established by large meta-analyses of randomized controlled trials and observational studies*." *See* Exhibit A (emphasis added). The abstract of an article in *Current Diabetes Reports* similarly noted in 2013 that ""[a] wealth of evidence has established that cholesterol-lowering statin drugs, widely used for the prevention of cardiovascular disease, do increase the risk of new-onset diabetes." *See* Exhibit B. How can it be that this conclusion is insufficiently reliable to be presented to a jury in this case, when it is considered reliable and significant enough to be reported to the scientific community?[1]

[1] Nor can Pfizer show that Lipitor is an exception to this effect. When the FDA ordered manufacturers of statins to add a warning about glucose elevation to the labels, it excepted pravastatin, but not atorvastatin, from this requirement. This is significant for two reasons. First, it shows that FDA did not simply sweep all statins into a single category without consideration of differences among them, and second, it shows that, when considering those differences, the FDA did not find (because the science does not show) that the effect does not occur at therapeutic doses of atorvastatin.

Pfizer would have this Court isolate each individual piece of evidence and require that each lone piece by itself prove causation. That would be improper. Contrary to Pfizer's repeated assertions, it is entirely proper to consider the totality of the evidence as opposed to requiring that each individual piece support an inference of causation. This is best exemplified by the holding in *Milward v. Acuity Spec. Prods. Gr., Inc.*, 639 F.3d 11 (1st Cir. 2011). *Milward* involved the appeal of the district court's barring of the causation opinion of plaintiff's toxicology expert. The excluded expert had employed a "weight of the evidence" methodology in attributing the cause of the plaintiff's leukemia to his benzene exposure. The Court of Appeals explained the district court's error as follows:

> At times, the court's error in excluding Dr. Smith's testimony derived from a mistake in its understanding of the weight of the evidence methodology employed by Dr. Smith. The court treated the separate evidentiary components of Dr. Smith's analysis atomistically, as though his ultimate opinion was *independently* supported by each. For example, the court referred to 'Dr. Smith's opinion that *because* benzene metabolites inhibit topo II and because some classes of topo II inhibitors appear to have a causal relationship to APL, *therefore* benzene has a causal relationship to APL.' *Milward*, 664 F.Supp.2d at 148 (emphasis added). This overstates Dr. Smith's conclusion as to the topo II evidence, and is indicative of an error in the court's understanding of the nature of Dr. Smith's analysis.
>
> In Dr. Smith's weight of the evidence approach, no body of evidence was itself treated as justifying an inference of causation. Rather, each body of evidence was treated as grounds for the subsidiary conclusion that it would, if combined with other evidence, support a causal inference. *The district court erred in reasoning that because no one line of evidence supported a reliable inference of causation, an inference of causation based on the totality of the evidence was unreliable.*

Milward, 639 F.3d at 7-8 (citing *NutraSweet Co. v. X–L Eng'g Co.*, 227 F.3d 776, 789 (7th Cir. 2000) (emphasis added) (holding that an expert's reliance on individual pieces of evidence, insufficient in themselves to prove a point, "did not render his opinion speculative"). Thus, the Court should resist Pfizer's attempts to divide and conquer each individual piece of evidence relied upon by Plaintiffs' experts in formulating their opinions that Lipitor causes diabetes at all four therapeutic doses. Rather, the Court

should consider the totality of the evidence and find that Plaintiffs' opinions are admissible because they are grounded in a reliable scientific methodology: the assessment and evaluation, with the requisite scientific expertise, of clinical trials, observational studies, and peer-reviewed published articles interpreting those studies

A. Pfizer's NDA Trials and Safety Updates Showed that Lipitor Increases Blood Glucose

1. Pfizer's NDA Trials

The vast majority of the data that Pfizer submitted with its New Drug Application came from trials involving the 10 mg dose of atorvastatin. [redacted] *See* Exhibit C and D. As noted in previous briefing, it was Pfizer and not Plaintiffs or Plaintiffs' experts, that identified the patients whose increases from their baseline glucose were deemed "clinically meaningful" in both the atorvastatin group and the placebo group. [redacted] *See* Exhibit E. Given that the difference between a normal glucose reading

and a diabetic glucose reading encompasses only 26 mg/dL, Dr. Wei's computations show that the magnitude of glucose elevation experienced in the NDA trials is sufficient to cause diabetes.

Although Pfizer contends that the difference between the atorvastatin group and the placebo group can be explained by a purported imbalance of patients with preexisting elevated levels of glucose, in fact that assertion does not explain the NDA results. Even assuming that Pfizer is correct that most of the patients identified as having clinically meaningful deviations had a high baseline glucose reading, that does not mean those patients were diabetic because a diagnosis of diabetes requires more than a single elevated plasma glucose level. Second, several of these trials suggest that atorvastatin reduces insulin sensitivity and elevates plasma glucose; these effects can eventually lead to diabetes. At a minimum, the results in the NDA trials suggest that Lipitor can elevate blood glucose, especially in patients who have had at least one elevated reading in the past. Third, Pfizer only included patients with meaningful changes in their glucose levels; elevated levels at baseline that remained at baseline elevated levels were not reported. But what is significant here is that these clinically meaningful deviations from baseline (as Pfizer defined them) occurred at the 10 mg dose of Lipitor. The NDA trials are thus consistent with other evidence that (a) Lipitor elevates blood glucose and (b) that it does so even at the lowest therapeutic doses.

[redacted]

Finally, although the FDA did not find the data in the NDA trials, standing alone twenty years ago, to provide sufficient evidence of glucose abnormalities to raise

concerns, in the context of all the evidence *now* available showing that statins in general, and Lipitor in particular, are associated with increased blood glucose and diabetes, the NDA trials provide important evidence that this effect is present at the 10 mg dose. Plaintiffs believe the evidence at the time of the NDA trials themselves ought to have raised concerns; even assuming the contrary, however, the data can now clearly be seen as part of the evidentiary picture establishing the effects of a 10 mg dose of Lipitor on blood glucose. In fact, Dr. Singh in his supplemental report concludes that the NDA trials showed "a statistically significant increase in clinically significant glucose elevations with both 10 mg and 80 mg of atorvastatin compared to placebo." *See* Exhibit H.

Pfizer argues that these studies – and the 1999 and 2001 Safety Updates described below - do not "fit" this case, because they address glucose changes and not diabetes, but as noted, this ignores the obvious connection between glucose changes and diabetes highlighted by Plaintiffs experts, and acknowledged by FDA in its approved labeling. The warning in the labeling does not even use the term "diabetes"; it states: "Increases in HbA1c and fasting serum glucose levels have been reported with HMG-CoA reductase inhibitors, including LIPITOR." FDA understands the "fit" quite clearly. Indeed, in updated labeling for Crestor (rosuvastatin) in 2013, the language was expanded to state:

> Increases in HbA1c and fasting serum glucose levels have been reported with HMG-CoA reductase inhibitors, including CRESTOR. *Based on clinical trial data with Crestor, in some instances these increases may exceed the threshold for the diagnosis of diabetes mellitus* [*see Adverse Reactions* (6.1)].

Exhibit T (emphasis added).

Pfizer's criticism that patients with baseline glucose levels in the diabetic range should have been excluded from analysis in the Pfizer clinical trial data is a position with which Plaintiffs and their experts continue to disagree for reasons that have been briefed ad nauseam. Pfizer did not exclude those patients from the safety tables to which the Plaintiffs' experts refer, and the glucose dysregulation is occurring in both normo- and hyper-glycemic patients. This is evidence of both the potential to promote new-onset

diabetes as well as to worsen existing diabetes. Contrary to Pfizer's assertion through typically selective quotation, Dr. Singh was aware there were patients with baseline glucose levels in the diabetic range and did *not* agree that patients with baseline glucose levels in the diabetic range should have been excluded from the analysis actually presented in the safety tables. *See* Exhibit U at 690:25 – 691:14; 695:20-24; 696:25 – 697:6; 715:12 – 716:11. Regardless, for many of the reasons cited by Pfizer, Dr. Singh himself made clear that the data from the atorvastatin safety summaries had to be interpreted with caution. It is nevertheless a piece of the overall picture that cannot and should not be ignored.

2. 1999 and 2001 Safety Updates

[redacted]

Plaintiffs' experts Dr. Quon and Dr. Singh both analyzed and discussed the Safety Updates in their supplemental reports. *See* Exhibit J at 49-57; and Exhibit H at 16-20. With respect to the 1999 Update, for example, Dr. Quon notes:

[redacted]

See Exhibit J at 50 (emphasis added). Dr. Quon likewise found that the 2001 Update provided "direct evidence that atorvastatin 10 mg causes substantial clinically meaningful hyperglycemia that inevitably over time promotes new onset diabetes or exacerbates existing diabetes." *Id.* at 51. Dr. Singh similarly found that the data from the 1999 and 2001 Safety Updates "indicate that, even when differences in exposure time are considered, the risk of developing a clinically meaningful glucose elevation with the 10 mg atorvastatin dose compared to placebo is significantly elevated." *See* Exhibit H at 20.

B. Dr. Quon's Studies Confirm the Effect of Lipitor on Glucose Levels

The glucose effects demonstrated by the NDA Trials and Safety Updates are further confirmed by the independent research of Plaintiffs' expert Dr. Quon. As more fully discussed in his supplemental report, Dr. Quon's own research – in large part conducted before this litigation began – shows that Lipitor causes and promotes "insulin resistance and hyperglycemia at various dosages which results in Lipitor causing new onset diabetes and the progression of existing diabetes." *See* Exhibit J at 5. In fact, since 2002, Dr. Quon published 38 papers on the clinical physiology of metabolic and vascular actions of statins. *Id. In no fewer than 15 of his peer-reviewed, published studies*, Dr. Quon "repeatedly cautioned that most statins including Lipitor (but excluding pravastatin) promote and cause insulin resistance and hyperglycemia which result in new onset diabetes and progression of existing diabetes." *Id.* at 5-6. Of particular note is the Koh et al. 2010 paper finding that all four doses of Lipitor significantly increased fasting plasma

insulin and glycated hemoglobin levels when compared to baseline or placebo. Lipitor at all four dosage levels was also found to decrease insulin sensitivity when compared with either baseline or placebo. In light of these findings, Dr. Quon and his co-authors concluded that "Lipitor treatment resulted in significant increases in fasting insulin and glycated hemoglobin levels consistent with insulin resistance and increased ambient glycemia in hypercholesterolemic patients at all doses tested in dose-dependent manner." *Id.* at 6. This particular paper was discussed in detail in Plaintiffs' previous briefing, *see* Docket #1159 at 5-7.

The studies by Dr. Quon and his co-authors are important for several reasons. While they do not assess new-onset diabetes as Pfizer complains, they provide important evidence on the potential mechanisms behind the role of statins in causing diabetes. This is specifically acknowledged by authors of other studies on statins and diabetes, including Navarese, et al. One cannot have diabetes without first having the adverse metabolic effects Dr. Quon and his co-authors found to be related to statin use. Moreover, the studies conducted by Dr. Quon and his co-authors, and importantly, the opinions Dr. Quon gleaned from them, were developed prior to this litigation and were contrary to his expectations. As Dr. Quon explained in his deposition, the findings he and his co-authors made regarding the adverse metabolic consequences of statins were actually unexpected and counter to the hypotheses they had going into the studies. *See* Exhibit K.

Pfizer argues that Dr. Quon's studies on statins and metabolic parameters should be ignored because they are too far removed from new onset diabetes. This argument – just like the argument that glucose increases should be ignored – is scientifically flawed given the relationship of the various metabolic parameters studied to new-onset diabetes. This relationship is fully set forth in Dr. Quon's supplemental report as noted in Plaintiffs' Supplemental Memorandum in Further Opposition to Pfizer's Motion to Exclude Plaintiffs' Expert Testimony on the Issue of General Causation. Again, this is evidence that cannot and should not be ignored. Moreover, Dr. Quon did not fail to consider

studies with inconsistent metabolic evidence as alleged by Pfizer. First, he specifically discussed most, if not all, of his own mechanistic studies with Dr. Koh. Further, while he did not cite the specific studies referenced in the 2011 Koh review paper that he co-authored and about which Pfizer is protesting, he indeed cited the review paper *itself*. That paper contains citations to 74 other publications including those Pfizer is complaining Dr. Quon ignored. A discussion of the details and findings of each citation in that review paper was clearly beyond the scope of this Court's directive in CMO 49. Notably, the authors of the review paper (including Dr. Quon) concluded:

> Experimental evidence clearly shows differential metabolic effects of distinct statins. These differential effects on hydroxymethylglutaryl-CoA reductase inhibition, isoprotenoid synthesis, calcium release, glucose transport, insulin secretion, and/or insulin resistance may help to determine overall adverse vs. beneficial metabolic actions. In addition, statins may be directly altering adiponectin levels independent of adiposity. Pravastatin increases expression of adiponectin mRNA, enhances adiponectin secretion, increases plasma levels of adiponectin, and enhances insulin sensitivity in mice and humans. Clinical studies and large scale randomized controlled trials demonstrate differences between individual statins, with pravastatin tending to reduce risk of new onset diabetes while atorvastatin, rosuvastatin and simvastatin together significantly increase this risk. Given the importance of preventing new onset diabetes and worsening of established diabetes, ongoing efforts in clinical and experimental settings to investigate these relationships are imperative. It is particularly important to investigate mechanisms underlying differential metabolic effects of various statins in patients at risk for metabolic diseases including diabetes, obesity, and metabolic syndrome.

Exhibit V at 6-7.

C. Pfizer's SPARCL, TNT and IDEAL Studies Show that Lipitor Causes Diabetes

Pfizer's own studies demonstrate that Lipitor causes diabetes. For example, SPARCL was a double-blind, randomized, placebo-controlled multi-center trial in which patients were randomized to high-dose (80 mg) atorvastatin or placebo. SPARCL's results were published in the New England Journal of Medicine (NEJM) in August 2006, but

those results did not include an analysis of any effect on glucose levels or diabetes. *See* Exhibit L at 13-14; Exhibit M at 25. Subsequent analyses of the SPARCL data, however, show an approximate two-fold significantly increased risk of diabetes among women, with a lower increased risk among men. *See* Exhibit M at 25; Exhibit N at 33.

Similarly, Pfizer's TNT clinical trial provides additional evidence that Lipitor can cause diabetes. [redacted]

[redacted]

Pfizer's IDEAL study also provides evidence that Lipitor causes diabetes. In this prospective, randomized, open-label, blinded end-point evaluation trial, patients were randomly assigned to receive a high dose of atorvastatin (80 mg/day; n = 4439), or a typical dose of simvastatin (20 mg/day, titrated up to 40 mg/day if necessary; n = 4449). The primary outcome was the occurrence of a major coronary event, defined as coronary death, confirmed non-fatal acute myocardial infarction ("MI"), or cardiac arrest with resuscitation. Patients were eligible for the IDEAL trial if they were 80 years of age or less, had experienced a definite MI, and qualified for statin therapy. 1,427 patients were excluded for known diabetes or a fasting blood glucose ≥ 126 mg/dL at baseline, leaving 7,461 (83.9%) of the original 8,888 patients for analysis. 239 of 3,737 patients randomized to atorvastatin 80 mg/day and 208 of 3,724 patients randomized to simvastatin 20 mg/day developed new-onset type 2 diabetes (6.40% vs. 5.59%, adjusted HR: 1.19, 95% CI: 0.98 to 1.43, p = 0.072). As noted by Dr. Quon, "This was greater than the number of cases of new onset diabetes caused by simvastatin 20 mg (which has lipid lowering ability comparable to 10 mg atorvastatin). It is likely that if there were a true placebo comparator

[redacted]

group, the relative risk of diabetes causation with 80 mg atorvastatin would have been even greater." *See* Exhibit J at 41.

Pfizer criticizes Plaintiffs' experts' analyses of SPARCL and TNT that demonstrate the increased risk of Lipitor causing diabetes at both the 80mg and 10mg doses. Pfizer's criticism is two-fold. First, Pfizer is critical of the analyses because they are based on *post-hoc* analyses. It is worth pointing out that when Pfizer was asked by MHRA to analyze its available clinical trial data on the diabetes issue, its response began not with the ASCOT study results which it presents as the be-all end-all in this Court, but instead with its own *post-hoc* analysis of IDEAL, SPARCL and TNT. Pls. Ex. 592, at 9. Second, Pfizer is now of the opinion that the Navarese meta-analysis that additionally considered PROVE-IT, IDEAL and ASCOT was a more appropriate meta-analysis to consider. Again, disagreement of experts as to what evidence or data are more compelling and each expert's decision to choose certain evidence or data are weight of the evidence issues for the jury to determine in deciding which expert to believe. Regardless, Drs. Singh and Roberts both considered Navarese in their initial reports, and found it supportive of their general opinions on statins increasing the risk of diabetes. That is indeed – contrary to Pfizer's position on what Navarese shows – what the authors of that meta-analysis conclude. Navarese, Meta-Analysis of Impact of Different Types and Doses of Statins on New-Onset Diabetes Mellitus (2013). While Pfizer cites Navarese as proof of no increased risk due to the apparent lack of statistical significance demonstrated by confidence intervals that cross 1.0, as the authors explain: "Because of the limited available direct evidence, large 95% Cis were found around the overall estimates; in contrast, the stability of the results in several probability and ranking analyses make the overall conclusions justified." Among those overall conclusions: 1) there was a gradient of risk for new-onset DM across different types and doses of statins; 2) pravastatin was numerically associated with the lowest risk, rosuvastatin with the highest, and atorvastatin intermediate; 3) the

findings were confirmed with moderate doses; and 4) for each statin, increased doses carried numerically higher risk compared with moderate doses. *Id*.

D. Pfizer's ASCOT Study Supports the Conclusion that Lipitor Can Cause Diabetes

Pfizer contends that its ASCOT trial, which has been the subject of substantial previous briefing, did not show a statistically-significant increased risk of diabetes. Plaintiffs' experts, however, believe that ASCOT provides important additional evidence of causation. For example, Dr. Quon opines that ASCOT "supports rather than detracts from the evidence" that atorvastatin promotes diabetes. *See* Exhibit J at 54. Dr. Singh, too, concluded that "the direction of effect [in the ASCOT study] is consistent with the increase in risk" of diabetes. *See* Exhibit H at 27. *See also* Docket #1384 at 7.

Pfizer criticizes Plaintiffs' experts for their views on the ASCOT study as published by Sever *et al*., though it is Pfizer's position in essence that this is the only available evidence on the issue of atorvastatin and diabetes – at least at 10mg. Pfizer would have this Court view the conclusion of Sever et al., and the affidavit of Dr. Harry Hemingway, as the last word on the subject. It is simply not. While Pfizer and its experts note the Sever authors as reporting no significant adverse effects on any secondary or tertiary endpoints (including diabetes), each fails to point out the acknowledgment of the Sever authors that: "The rates of life-threatening arrhythmias, heart failure, renal impairment, and new onset diabetes were, however, marginally increased among patients receiving atorvastatin, but the differences were based on small numbers of events and are probably the result of chance variation." *See* Exhibit W at 1154-55 (emphasis added). The Sever authors thus acknowledged both a numerical increase in diabetes cases in the atorvastatin group and a lack of power to detect a true difference in some of the tertiary endpoints. As noted by Dr. Singh, ASCOT was powered to find a statistically significant difference – if one existed – on the primary endpoints, not secondary or tertiary endpoints. *See* Exhibit U at 585:19 – 586:4. [redacted]

[redacted]

E. Meta-Analyses and Observational Studies Confirm that Lipitor Can Cause Diabetes

Numerous meta-analyses and observational studies further confirm that Lipitor causes diabetes. Unlike observational studies, meta-analyses involve randomized clinical trials; the meta-analysis adds the perspective of combining multiple studies and looking at them together. As Plaintiffs have previously described, the following published meta-analyses further support Plaintiffs' experts' opinions that Lipitor causes diabetes:

- Rajpathak SN, Kumbhani DJ, Crandall J, Barzilai N, Alderman M, Ridkcr PM. Statin therapy and risk of developing type 2 diabetes: a meta-analysis. DIABETES CARE. 2009;32:1924
- Sattar N, Preiss 0, Murray HM, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomized statin trials. LANCET. 2010;375:735-42
- Mills EJ, Wu P, Chong G, Ghcment I, Singh S, Aki EA, Eyawo 0, Guyatt G, Berwanger 0, Briel M. Efficacy and safety of statin treatment for cardiovascular disease: network meta-analysis of 170,255 patients from 76 randomized trials. QJM. 2011 ;104: 109-24
- Naci H, Brugts J, Ades T. Comparative tolerability and harms of individual statins: a study-level network meta-analysis of 246,955 participants from 135 randomized controlled trials. Circ CARDIOVASC QUAL OUTCOMES. 2013;6:390-9
- Coleman CI, Reinhart K, Kluger J, White CM. The effect of statins on the development of new-onset type 2 diabetes: a meta-analysis of randomized controlled trials. CURR MED RES OPIN. 2008;24:1359-62

[redacted]

- Preiss D, Seshasai SR, Welsh P, Murphy SA, *et al*. Risk of incident diabetes with intensive-dose compared with moderate dose statin therapy: a meta-analvsis. JAMA.2011;305(24):2556-64

Apart from the aforementioned meta-analyses, Plaintiffs' experts also relied upon numerous observational studies. Pfizer takes issue with these studies, individually and collectively, but, as discussed below, Plaintiffs' experts' use of these published studies, in addition to other evidence, does not render their opinions unreliable. The observational studies on which Plaintiffs' experts rely, and the significance of which Pfizer disputes, include:

The Cederberg Paper: This paper, published in May of 2015, has been previously described for the Court. *See* Plf. Supp. Mem. (Doc. # 1159) at 4-5. *See also* Exhibit Q. As previously described, not only did Cederberg find increased risk of diabetes at 20 and 40 mg of atorvastatin and increased insulin resistance and impaired beta-cell function at 10, 20, and 40 mg doses of atorvastatin, it also found increased risk of diabetes at doses of simvastatin that can be considered equivalent to the 10, 20 and 40 mg doses of atorvastatin. Moreover, because the study described in the Cederberg paper involved only men, it would be expected that the magnitude of the effects seen would be greater in women. The Cederberg paper was considered and relied upon by Drs. Quon, Singh and Roberts in formulating their opinions that Lipitor causes diabetes across all therapeutic dosages.

Pfizer offer numerous criticisms of the Cederberg paper, but the fact that some experts do not agree with the conclusion of a particular peer-reviewed published article, or the fact that a study may not be perfect (no studies are) does not mean that the study cannot provide valid and reliable support for the conclusions of Plaintiffs' experts. Dr. Quon states that it is "among the most robust and important papers with respect to outcome studies related to the issue of statins, including atorvastatin, causing diabetes," and explains why:

> The reason that this study is so significant to the issue of statins and diabetes is that it is the first large prospective outcome study whose primary aim is to evaluate risk of diabetes in response to statin treatment. In addition, the investigators employed metabolic testing that allowed them to accurately and sensitively evaluate both changes in insulin resistance and insulin secretion to provide mechanistic insight into how many statins including atorvastatin are causing diabetes.

See Exhibit J at 46-47.

Moreover, the Cederberg paper also "discusses in a cogent manner why other studies may have underestimated the magnitude of the effect of statins to cause new onset diabetes." *Id.* at 47. Indeed, Dr. Quon concludes:

> [T]he Cederberg paper is a landmark paper directly addressing the ability of statins including atorvastatin and simvastatin at lipid lowering doses equivalent to atorvastatin to cause diabetes. The study is large, robustly designed and executed, and the data and conclusions are unequivocal that atorvastatin at 40 and 20 mg causes substantial new onset diabetes in a significant number of patients due to increased insulin resistance and impaired insulin secretion in a dose-dependent manner.

See Exhibit J at 48. Dr. Singh, too, found the Cederberg paper relevant and helpful in reaching his conclusions concerning Lipitor and diabetes, particularly with respect to 20 mg and 40 mg doses. *See* Exhibit H at 9-10, 32. Thus, while Pfizer seeks to distinguish and dismiss this important study, its criticisms should be presented to a jury; they provide no basis to preclude Plaintiffs' experts from telling a jury about this scientific study and the peer-reviewed published paper reporting it.

The Carter Paper: This paper reports on a retrospective cohort study using information from Canadian databases. Over the 14-year study period, the study authors identified 471,250 patients with no history of diabetes who were newly treated with a statin. Furthermore, the authors made adjustments for confounders including age, gender, year of cohort entry, history of cardiac disease and cardiac procedures, Charlson comorbidity index, and history of medication use (including medications with an impact on glycemic control) in the past 12 months. Analysis of the data showed increased risk of diabetes in patients taking moderate doses – that is at least 20 mg, but less than 80 mg

– and high doses – at least 80 mg – of atorvastatin, and thus implies causation at the 20 mg and 40 mg doses of Lipitor.

Dr. Singh discussed both the strength and limitations of the Carter paper in his supplemental report. For example, he clearly stated that the fact that the three comparators (high, mid and low dose) included both Lipitor and other statins of similar potency made it impossible to separate the effect of one statin from another. He also noted that the lack of a non-user arm prevented evaluation of lower potency statins such as 10 mg Lipitor. However, despite these recognized limitations, Dr. Singh found scientific value in the authors' conclusion that "moderate dose and high potency statins carry a higher risk of type 2 diabetes than low potency statin[s]." *See* Exhibit H at 8.

On the other hand, Pfizer's criticisms of the Carter paper are not really criticisms at all. Rather, they merely demonstrate a disagreement on how to interpret the paper's results. For example, Pfizer's principle attack – which relies on its own expert's report – is that "the most plausible" explanation for increased relative risk for each statin by dose in confounding by indication. *See* Docket #1383 at 22. However, Pfizer's plausible alternative is merely that – an alternative explanation – which cannot form the basis for disregarding its evidentiary value. The parties' respective experts have differing opinions on the implications of the strengths and limitations of the study. Such disagreements are not matters of law that can, or should, be determined by the Court.

The Chen Paper: The Chen Paper describes a case-control study using a Taiwanese database, in which 1065 cases (female patient with new onset diabetes between January 1, 2004 and December 31, 2006) and 10,650 controls were analyzed to determine the risk of diabetes among women using the WHO recommended daily dose approach to assess dose responsiveness. The study analyzed the effect of cumulative dose in terms of "low," "moderate," and "high" doses of atorvastatin which fairly translate into the traditional 10 mg, 20 mg, 40 mg, and 80 mg doses.

It is important to note that, despite Pfizer's continued attacks on observational studies for the potential for confounding, the study *did*, in fact, adjust for a number of important variables, including: age, gender, comorbidities (history of hypertension, coronary artery disease, diabetes, hyperlipidemia, atrial fibrillation, chronic kidney disease, obesity and peripheral arterial disease), level of urbanization, region of residence, socioeconomic status, and use of medication. Rather, Pfizer's only criticism, which relies exclusively on its own expert reports for support, is that the study did not adjust for *every* potential variable that Pfizer could imagine. However, Plaintiffs' burden here is not to resolve the criticisms of Pfizer's expert. Rather, it is the Court that is the gatekeeper here, not Pfizer's Dr. Hennekens.[3]

Aside from Pfizer's superficial attacks, the study identified an increased risk of diabetes at all three levels (low dose, medium dose, and high dose) in two out of three age groups studied. *See* Exhibit R at 6. This finding is particularly significant for the Court's purposes here for two reasons: First,, it is consistent with the results of the Navarese meta-analysis which entitles it to greater scientific weight; and second, as stated by Dr. Roberts, "it shows that even exposure to low accumulated doses of atorvastatin increased the risk of NOD in women." *See* Exhibit S at 7. More specifically, even the highest cumulative dose considered in the study (cDDD > 60) – which was associated with more than a three-fold increased risk of diabetes – would be achieved by an individual that had taken the *10 mg dosage for only 2 months*. *See* Exhibit H at 25.

The Culver Paper: The Culver paper reports on an analysis of the Women's Health Initiative ("WHI") data. Culver found that statin use increased the risk of diabetes; the paper also breaks down the risk by statin, allowing comparisons among statins and controlled for a number of confounding factors including age, race/ethnicity, education,

[3] Ironically, Pfizer seems to adopt Dr. Singh's belief that temporality is a "very important criteria" for causation for the convenience of its position here. However, it took Dr. Murphy to task for allegedly relying on temporality in her report.

cigarette smoking, BMI, physical activity, alcohol intake, energy intake, family history of DM, hormone therapy use, study arm, self-report of hypertension, and self-report of CVD. *See* Exhibit Y at 148. The authors further conducted several sub-group analyses to *control for confounding by indication* (thus, negating Pfizer's over-arching argument that such studies are unreliable) and using a prospective design which allowed the authors to examine temporality (once again, negating any criticism that this "very important criteria" was absent). In the end, Pfizer's only true criticism of the Culver paper is not that it did not adjust for variables – only that it did not adjust for *every conceivable* variable.

The Culver paper is important to the Court's analysis because it allows comparisons based on the potency of the different statins. Like atorvastatin, simvastatin was found to increase of diabetes. Notably, the highest dose of simvastatin, 80 mg, is generally considered to be dose-equivalent to a 40 mg dose of atorvastatin. Thus, even if all the women in the WHI study were taking the highest dose of simvastatin, at a minimum, this would suggest that moderate doses of atorvastatin also cause diabetes. Plaintiffs' expert Dr. Singh specifically discussed the importance of the Culver paper and termed it "relevant to support the finding that high potency statins such as atorvastatin are also associated with an increase in the risk of diabetes among women." *See* Exhibit H at 8.

Pfizer insists that Plaintiffs' experts' use of observational studies renders their causation opinions inadmissible, because, it claims, such studies cannot show causation as they are merely "hypothesis testing." This is simply not true. Observational trials are a form of epidemiological experiment recognized in the Reference Manual for Scientific Evidence. They provide evidence of causation, although it is well-recognized that, standing alone, they do not provide the kind of strong evidence for causation that can be found in a randomized clinical trial. See RMSE at 218. Pfizer also criticizes the particular limitations of each of those observational studies, most of which are highlighted by the studies' authors themselves. However, each of the studies also has particular strengths

which make them worthy of consideration, especially given the limitations of the randomized clinical trial evidence on the issues. For example, some of the studies provide limited information on certain doses, but that does not preclude their consideration on others. Further, some combine doses making it difficult to quantify risk at a particular dose, but still providing information on dose-response generally. However, the observational studies so criticized by Pfizer's experts are *all published in peer-reviewed medical journals*. While one may quibble with their shortcomings, or even the authors' conclusions, they are unquestionably the type of data relied upon by experts in the field, and often in court as well. As the Reference Manual on Scientific Evidence observes: "The bulk of the statistical studies seen in court are observational, not experimental." REF. MAN. SCI. EVID. at 220. As it further notes:

> Observational studies can produce legitimate disagreement among experts, ad there is no mechanical procedure for resolving such differences of opinion. In the end, deciding whether associations are causal typically is not a matter of statistics alone, but also rests on scientific judgment.

Id. at 222. Plaintiffs' experts have reliably and justifiably brought their judgment to bear on the observational studies cited in their reports.

But this makes little difference because none of Plaintiffs' experts relies on observational trials alone in reaching an opinion of causation. Rather, the use of these observational trials is confirmatory, providing even greater assurances that associations found in clinical trials and other evidence are in fact causal. Dr. Singh, a practicing epidemiologist, addresses this very point in his initial Report:

> [R]andomized clinical trials are not necessary to establish causal evidence of harm since they cannot be conducted in all circumstances. There is no mechanism by which to randomly assign participants for non-modifiable exposures. The event may be sufficiently rare to be evaluated in a randomized trial. Absent such placebo-controlled trials to address this question, we rely on meta-analysis of randomized controlled trials to determine causation. Observational studies are often used in this setting.

See Exhibit M at 5. Plaintiffs' experts properly considered the wealth of observational studies, giving them the weight they deserve and placing them in context with the clinical trials and meta-analyses to reach a judgment about causation.

Furthermore, differing views about the strengths of various studies are not a basis to exclude expert testimony. *Knight v. Kirby Inland Marine Inc.*, 482 F.3d 347, 354 (5th Cir. 2007) (because, in epidemiology "hardly any study is ever conclusive," experts are not required to support their opinions with studies that "unequivocally support their conclusions"); *United States v. Bonds*, 12 F.3d 540, 561 (6th Cir. 1993) ("[a]bsolute certainty of result or unanimity of scientific opinion is not required for admissibility."); *In re Vioxx Products Liab. Litig.*, 401 F. Supp. 2d 565, 599 (E.D. La. 2005) (where both sides relied on same scientific material, but interpreted it differently and came to different conclusions, expert testimony from both sides was admissible); *Beck v. Koppers, Inc.*, No. 03-cv-60, 2006 WL 270260, *5 (N.D. Miss. Feb. 2, 2006) (failure of expert to specify weight accorded to various studies did not render ultimate judgment about the overall weight of the scientific evidence inadmissible). Pfizer clearly disagrees with the weight that Plaintiffs' experts have accorded to the various studies they considered. But that disagreement is a subject to explore on cross-examination, not a basis to exclude these qualified experts from testifying to the opinions they formed after consideration of all the scientific evidence.[4]

[4] Plaintiffs have not here discussed the evidence from studies of other statins that further supports the conclusion that Lipitor causes diabetes. That evidence is discussed in prior submissions, to which Plaintiffs respectfully refer the Court. Plaintiffs note, however, that Pfizer continues to insist that *no* evidence of a causal relationship exists, even at the 80 mg. dose, the fact that a near-class-wide effect (involving all statins except pravastation) has been shown is yet another factor supporting the reliability of the opinions of Plaintiffs' experts that Lipitor, like other statins, is capable of causing diabetes.

II. PLAINTIFFS' EXPERTS PROPERLY CONCLUDE THAT LIPITOR CAN CAUSE DIABETES AT DOSES BELOW 80 MG

As Plaintiffs pointed out in their Supplemental Memorandum in Further Opposition to Pfizer's Motion to Exclude Plaintiffs' Expert Testimony on the Issue of General Causation (Docket #1384), the supplemental reports of Drs. Quon, Singh, and Roberts provide sufficient and reliable evidence that Lipitor can cause diabetes at 10 mg, 20 mg, and 40 mg, as well as at the 80 mg dose. In reaching their conclusions, Drs. Quon, Singh, and Roberts considered much of the same evidence they used to form their original opinions concerning Lipitor and diabetes. Specifically, of the evidence discussed above, the original NDA Studies, the 1999 and 2001 Updates, the TNT and IDEAL studies, the ASCOT study, the Koh/Quon studies, and many of the observational studies support causation not only at 80 mg, but also at the other therapeutic doses as well. Drs. Quon, Singh, and Roberts specifically considered this evidence through the lens of dosage, as well as their original perspective on general causation, and found sufficient evidence to conclude that causation occurs at the lower therapeutic doses.

Pfizer provides no legitimate basis to exclude these opinions. Indeed, while Pfizer claims that the opinions of Plaintiffs' experts are methodologically unsound, in fact the methodology used is precisely the same as the methodology used by Defendants' experts: consideration and analysis of the published papers and studies. Indeed, alone among the experts for either side, Dr. Quon has himself performed some of the studies at issue; the remainder of the experts, both for Pfizer and for Plaintiffs, have reviewed the literature, identified and analyzed relevant studies, and drawn a conclusion about the extent to which these studies demonstrate that Lipitor can cause diabetes at doses less than 80 mg. That Plaintiffs' experts weight the studies differently and reach a different conclusion from Pfizer's experts provides no basis to exclude their opinions.

Moreover, in this context, it must be noted that although each of Pfizer's experts criticize Plaintiffs' experts for failing to consider the totality of available evidence,

Plaintiffs' experts were specifically precluded by the Court, as reflected in CMO 49, from considering the totality of available evidence: "An expert may only consider and rely on studies or data submitted to the Court in response to its September 28, 2015 text order, (see Dkt. Nos. 1153, 1159), or specifically cited in an expert's prior report." Indeed, Pfizer has moved to strike Dr. Roberts' supplemental report because it cited a study not previously cited by her – but cited by other experts – and because it contained a quotation from a review paper not previously cited.

Nor do the specific criticisms Pfizer addresses to the evidence of causation at doses below 80 mg provides a basis to exclude Plaintiffs' experts' opinions. As discussed above, these criticisms reflect scientific disagreements, but do not reflect any flaw, methodological or otherwise, in the evidence, nor in the conclusions of Plaintiffs' experts that Lipitor causes diabetes at all therapeutic doses. Rather, as outlined in Plaintiffs' prior briefing, the various lines of evidence discussed and analyzed in the supplemental reports of Dr. Quon, Singh, and Roberts provide reliable scientific evidence that Lipitor causes increases in glucose and other adverse metabolic consequences as well as new-onset diabetes at doses less than 80 mg, including the lowest therapeutic dose of 10mg.

III. THE DISAGREEMENT BETWEEN THE PARTIES' EXPERTS ABOUT THE MEANING OF THE SCIENTIFIC EVIDENCE HERE CANNOT PROPERLY BE RESOLVED BY THE COURT

The Court should decline to accept Pfizer's invitation to act as a fact-finder under the guise of *Daubert*. Seen for what they are, Pfizer's criticisms of Plaintiffs' experts are merely disagreements with the weight they afford to particular types of evidence – such as observational studies – and the conclusions they draw from that evidence. Circuit courts routinely warn district courts against over-reaching when conducting their gate-keeping responsibilities because it "would elevate them to the role of St. Peter at the gates of heaven, performing a searching inquiry into the depth of an expert witness's soul—separating the saved from the damned. Such an inquiry would inexorably lead to

evaluating witness credibility and weight of the evidence, the ageless role of the jury." *McCullock v. H.B. Fuller Co.*, 61 F.3d 1038, 1045 (2d Cir. 1995).

Pfizer, however, explicitly asks this Court to delve into factual issues of weight and credibility that should be properly reserved for the jury. The Court's mandate to consider the *scientific* reliability of expert testimony should not be confused – as Pfizer does here – with the jury's role in determining its *ultimate* reliability:

> It must be emphasized, however, that the *Daubert* inquiry into "reliability" is separate and distinct from the ultimate issue for the jury's consideration, i.e. whether plaintiffs have submitted sufficiently "reliable" proof to permit them to satisfy their burden of proof in a particular case. There is sufficient similarity between the *Daubert* inquiry and a jury's inquiry that a real danger exists that a court will conflate the two and, thereby, improperly assume the factfinder role which is appropriately reserved for the jury.
>
> Juries decide, on a daily basis, that a particular litigant's proof (including his expert testimony) on a specific issue is not "reliable" in the sense of being persuasive and worthy of credence. This is not a breakdown of the civil justice system; it is the civil justice system. The fact that a jury might ultimately decide that a particular expert's testimony is unreliable does not mean, however, that a court acted improperly in permitting the jury to consider that testimony in the first place. This court's proper inquiry in the *Daubert* context is whether the expert's testimony is so lacking in reliability as to preclude that expert from even presenting his testimony to the jury. This is, very clearly, a different issue than the ultimate issue for the jury, and this court must be careful not to confuse the two.

Pers. v. Ford Motor Co., No. 3:09CV133-MPM-DAS, 2011 WL 10501606, at *3 (N.D. Miss. Oct. 13, 2011). *Daubert* does not permit, much less require, the Court to resolve conflicting interpretations of scientific evidence as Pfizer seems to propose. Such analytical disagreements should be left to the juries. *Ambrosini v. Labarraque*, 101 F.3d 129, 141 (D.C. Cir. 1996) ("By attempting to evaluate the credibility of opposing experts and the persuasiveness of competing scientific studies, the district court conflated the questions of the admissibility of expert testimony and the weight appropriately to be accorded such testimony by a fact finder."); *Ferebee v. Chevron Chem. Co.*, 736 F.2d 1529, 1535 (D.C. Cir. 1984) ("The experts on both sides relied on essentially the same diagnostic methodology;

they differed solely on the conclusions they drew from test results and other information. The case was thus a classic battle of the experts, a battle in which the jury must decide the victor."); *City of Pomona v. SQM N. Am. Corp.*, 750 F.3d 1036, 1049 (9th Cir.) cert. denied sub nom. *SQM N. Am. Corp. v. City of Pomona, Cal.*, 135 S. Ct. 870, 190 L. Ed. 2d 703 (2014) ("A factual dispute is best settled by a battle of the experts before the fact finder, not by judicial fiat. Where two credible experts disagree, it is the job of the fact finder, not the trial court, to determine which source is more credible and reliable.").

The evidence before the Court demonstrates that there is, at most, a scientific disagreement between experts on how to interpret clinical data and peer-reviewed journal articles. Yet Pfizer asks the Court to be the scientific arbiter and make a substantive decision on the merits of the parties' respective positions and the implications of the evidence. However, the Court's role is not to wade into a battle of the experts and pick winners and losers. It is merely to make sure that everyone is following the rules.

The Fourth Circuit recently made this very point when it reversed a district court that engaged in the kind of improper fact-finding that Pfizer invites here. In *Reyazuddin v. Montgomery Cty., Maryland*, the court noted that the parties' experts were both qualified as experts, yet drew opposing conclusions on the potential costs of providing an employee certain accommodations under the American with Disabilities Act. 789 F.3d 407, 417 (4th Cir. 2015). But rather than allowing a jury to resolve the dispute, the Fourth Circuit found that the district court had "improperly weighed conflicting evidence" by stating that the plaintiff's expert's opinion was "unsupported" thereby giving greater evidentiary value to the defendant's expert's testimony. Since the experts' respective opinions on conflicting evidence "set[ ] up a battle of the experts," it should not have been resolved by the district court.[5]

[5] That *Reyazuddin* involved a motion for summary judgment, rather than a motion to exclude under Rule 702, only reinforces the point, for the Court is no more authorized to

The result should be no different here. The Court should allow a jury to determine the credibility, weight, and ultimate reliability of Plaintiffs' experts' opinions, as required by Rule 702 and *Daubert,* rather than making improper factual determinations. Attacks on the weight that Plaintiffs' experts afford particular types of evidence - whether it is clinical trial data or observational studies – is an issue that Pfizer can raise on cross examination. Factual inquiries, even those cloaked methodological criticisms, should not be resolved as a matter of law. *In re Toyota Motor Corp. Unintended Acceleration Mktg., Sales Practices, & Products Liab. Litig.*, 978 F. Supp. 2d 1053, 1070 (C.D. Cal. 2013).

CONCLUSION

For the foregoing reasons, this Court should deny in its entirety Pfizer's motion to exclude evidence of general causation.

February 19, 2016

Respectfully Submitted,

/s/ H. Blair Hahn
H. Blair Hahn (Fed. I.D. # 5717)
RICHARDSON PATRICK
WESTBROOK & BRICKMAN, LLC
1037 Chuck Dawley Blvd., Bldg. A
Mount Pleasant, SC 29464
bhahn@rpwb.com
Telephone: (843) 727-6500
Facsimile: (843) 727-6642

Plaintiffs' Lead Counsel

Jayne Conroy (NY 8611)
SIMMONS HANLY CONROY
One Court Street
Alton, IL 62002
Telephone: (618) 259-2222
Facsimile: (618) 259-2251

act as a factfinder on a *Daubert* motion than on a summary judgment motion. Indeed, whether the Court finds an expert persuasive is of *less* significance when the Court acts as a gatekeeper under Rule 702 than when it determines, under Fed. R. Civ. P. 56, whether genuine issues of disputed fact preclude summary judgment.

jconroy@simmonsfirm.com

Ramon Rossi Lopez
LOPEZ MCHUGH, LLP
100 Bayview Circle, Suite 5600
Newport Beach, CA 92660
Telephone: (949) 737-1501
Facsimile: (949) 737-1504
rlopez@lopezmchugh.com

Plaintiffs' Executive Committee on behalf of the Plaintiffs' Steering Committee